

FREQUENTLY ASKED QUESTIONS ABOUT AVIAN INFLUENZA

Avian Influenza, or "bird flu", is a contagious disease of animals caused by viruses that normally infect only birds and, less commonly, pigs. Avian Influenza viruses are highly species-specific. On rare occasions, these viruses cross the species barrier to infect humans. The infection of domestic poultry with avian influenza viruses causes two main forms of disease with either high or low extremes of virulence. The so-called "low pathogenic" form commonly causes only mild symptoms with ruffled feathers and a drop in egg production that may go undetected. The highly pathogenic form, known as highly pathogenic avian influenza (HPAI) is far more virulent, spreading rapidly through poultry flocks, affecting multiple internal organs with a mortality that approaches 100%, often within 48 hours.

What are the HPAI viruses?

There are many different subtypes of type A influenza viruses. These subtypes differ because of certain proteins on the surface of the influenza A virus (hemmagglutinin HA and neuraminidase NA proteins). There are 16 different HA subtypes and nine different NA subtypes of influenza A viruses. Each combination is a different subtype. All known subtypes of influenza A viruses can be found in birds.

To date only the H5 and H7 subtypes are known to cause the highly pathogenic form of the disease. However, not all viruses of the H5 and H7 subtypes are highly pathogenic, causing severe disease in poultry. It appears that the H5 and H7 viruses are introduced to poultry flocks in their low-pathogenic form. When allowed to circulate, these viruses mutate within a few months into the highly-pathogenic form. This is the reason for concern with the presence of the H5 or H7 virus in poultry even when initial signs of infection are mild.

How might HPAI be spread?

Wild waterfowl are the natural reservoir of all influenza A viruses. They have probably carried influenza viruses, including H5 and H7 subtypes in the low pathogenic form with no apparent harm for centuries. Evidence now suggests that migratory birds can introduce low pathogenic H5 and H7 viruses into poultry flocks and these then mutate to the highly pathogenic form. HPAI viruses have been isolated from migratory birds on rare occasions after these birds have been found dead within flight range of a poultry outbreak. Recent events indicate that some migratory birds are now spreading the H5N1 virus in the highly pathogenic form and will continue to spread it.

Are current outbreaks in poultry significant?

The current outbreak of HPAI that began in South East Asia in mid-2003 is the largest and most severe on record. Never before in history have so many countries been simultaneously affected resulting in the loss of so many birds. The H5N1 virus is the causative agent and has proved to be very tenacious despite efforts to limit or destroy the virus. H5N1 is now considered endemic in parts of Indonesia, Vietnam, Cambodia, China, Thailand and probably Laos. Control of this disease is expected to take several years.

Which countries have had poultry outbreaks?

From mid-December 2003 through early February 2004, first ever recorded HPAI poultry outbreaks caused by H5N1 were reported in the Republic of Korea, Vietnam, Japan, Thailand, Cambodia, Lao People's Democratic Republic, Indonesia and China. In August 2004, Malaysia was added to the list followed by Russia in July 2004. Deaths of wild migratory birds from the H5N1 virus were reported in August of that year in Kazakhstan and Mongolia. In October 2005, H5N1 was confirmed in poultry in Turkey and Romania with outbreaks in wild and domestic birds under investigation in Croatia, Greece and Macedonia. More countries are likely to continue reporting detection and outbreaks of H5N1. Japan, the Republic of Korea and Malaysia have announced control of their poultry outbreaks and are now considered free of the disease but HPAI continues in other areas with varying degrees of severity.

How might human health be affected?

A widespread persistence of H5N1 in poultry populations poses two main risks for human health: (1) direct infection when the virus passes from poultry to humans with resultant severe illness and (2) a greater concern is that the virus will change into a form that is highly contagious among humans and begin to spread easily from person to person, starting a global outbreak (pandemic).

Of the few avian flu viruses that have crossed the species barrier to infect humans, H5N1 has caused the most severe disease and largest number of deaths. Unlike the seasonal human influenza which causes only mild respiratory symptoms in most persons, influenza caused by the H5N1 virus usually follows a very aggressive clinical course with a high mortality rate (approximately 50%). Death is usually from viral pneumonia and multi-organ failure and occurs most commonly in previously healthy children and young adults.

Where and how many human cases have occurred?

Hong Kong experienced the first H5N1 virus outbreak in humans in 1997 with 18 cases and six deaths. In early 2003, the virus caused two infections and one death in a family in Hong Kong who had recently traveled to southern China. There had been no cases in humans elsewhere in the world until that time. Since 2003, the outbreak has resulted in 121 laboratory-confirmed human cases with 62 deaths reported in four countries: Cambodia, Indonesia, Thailand and Viet Nam.

How are people infected?

The main route of human infection is direct contact with infected poultry or surfaces and objects contaminated with their feces or blood. To date, most human cases have occurred in rural and periurban areas where households keep small poultry flocks that roam freely, often entering homes and sharing children's outdoor play areas. Large quantities of the virus are excreted in the feces of infected poultry. In countries where poultry is relied upon for income and food, families slaughter and consume birds that are ill. Exposure occurs during slaughtering, defeathering, butchering and preparation of poultry for cooking. Infection in humans occurs with consumption of inadequately cooked poultry or raw poultry products such as duck's blood. There is no evidence that properly cooked poultry or eggs are a source of infection.

Is the virus spread easily from birds to humans?

No. Only 121 cases have occurred in the current outbreak despite huge numbers of birds being affected and numerous associated opportunities for human exposures, especially in backyard flocks. It is not understood why some people but not others become infected with similar exposures.

What is a pandemic?

A pandemic may occur when three conditions have been met: a new influenza virus subtype emerges; it infects humans causing serious illness; and it spreads easily and sustainably among humans. The H5N1 virus meets the first two conditions. The risk that it will acquire the ability to have efficient and sustained human-to-human transmission is present as long as opportunities for human infections occur. These opportunities will persist as long as the virus continues to circulate in domestic birds, perhaps for years to come.

How can the H5N1 virus become a pandemic virus?

The H5N1 virus can improve its ability to infect humans when "reassortment" occurs, resulting in a new virus with enhanced human transmissibility. This is caused by an exchange of genetic material between human and avian influenza viruses when

a human becomes infected with both at the same time. Pigs may also serve as "mixing vessels" for this exchange and then transmit the new virus to humans. Such an event would be announced by a sudden surge of cases with explosive spread. A more gradual process of "adaptive mutation" might allow the virus to develop the ability to efficiently bind to human cells. With subsequent infections to humans, adaptive mutations would appear as small clusters of human cases with some evidence of human-to-human transmission. This slower mechanism would give the world more time to take defensive action.

Has human-to human transmission occurred yet?

Human-to-human transmission cannot be ruled out in a family cluster of cases that appeared in Vietnam in January 2004 and in another family cluster in March. In January 2005 a girl in Thailand probably passed the virus to her mother. In no instance has the virus spread beyond the first human-to-human contacts or caused illness in the general community. This sort of transmission requires very close sustained contact with an ill person. The overwhelming majority of cases that have turned up in families have been traced to common exposures to birds rather than to other infected humans. The World Health Organization has not changed its overall assessment of the pandemic risk. Health care workers treating H5N1 patients, who have taken normal precautions, have not come down with bird flu.

How serious is the current pandemic risk?

The H5N1 virus is now firmly entrenched in poultry in large parts of Asia. As a result, more human cases will occur and provide the virus increasing opportunities for "reassortment", increasing the risk of the emergence of an easily transmissible human pandemic strain. The recent spread in wild birds and poultry to new areas also allows increased opportunities for human cases to arise in an expanding geographic range, increasing the probability that a pandemic will occur.

What other concerns are present?

Domestic ducks excrete large quantities of the highly pathogenic H5N1 virus without showing signs of illness, acting as silent reservoirs for the virus. The H5N1 virus circulating now is more lethal in experimentally infected mice and ferrets when compared to the H5N1 from 1997 and 2004. The H5N1 has expanded its hosts, infecting and killing mammalian species previously resistant, for example, tigers in the Bangkok Zoo who were fed raw ill birds.

The behavior of the virus in its natural reservoir, wild waterfowl, may be becoming more lethal causing a spring 2005 die-off of migratory birds in China.

What are the major reasons for concern over the possibility of a pandemic?

Computer modeling in Thailand suggests the possibility, with immediate early aggressive coordinated international intervention, of stopping a potential pandemic strain. This would be analogous to quenching a small fire with forest-fire potential. Once human-to-human transmission reaches a major metropolitan area, however, the past history of influenza pandemics indicates that spread throughout the entire world can be expected to occur in only a matter of weeks. Most health authorities doubt that it will be able to be stopped, once a pandemic is underway, only mitigated, at best. A pandemic virus will be spread rapidly by the coughing or sneezing by infected persons. Unlike SARS, individuals shed the virus for about two days before symptoms appear. Asymptomatic air travelers will be very difficult to screen because spread may occur without fever. Attack rates during a pandemic, by definition, reach 25-35% of the total population. Even with a mild pandemic virus, such as occurred with the 1957 "Asian flu" global death rates were in the neighborhood of two to 7.4 million deaths. The 1918 pandemic caused over 40 million deaths with a mortality rate of 2.5%. Presently known mortality rates among humans confirmed to be infected with H5N1 are extremely high by historic standards, in excess of 50%. It is true that this number does not take into account a denominator made larger by those with less severe infections who never present to health authorities. It is also hoped that in becoming more easily transmissible, a pandemic virus will lose a great deal of its lethality. A pandemic is expected to cause large surges of people seeking or requiring hospitalization, temporarily overwhelming health services. High rates of worker absenteeism can interrupt other essential services such as law enforcement, transportation, and communications. These social and economic disruptions may be temporary if the rates of illness peak rapidly, however, today's closely interrelated systems of trade and commerce may amplify the disruptions. It is expected that a second wave of global spread would occur within a year of the first during which those who were ill and survived the first wave could once again become sick during the second. Three such waves occurred during the 1918 pandemic.

What are some warning signals that a pandemic might be about to start?

The most important signal will be the appearance of clusters of patients with clinical influenza suggesting H5N1, closely related in time and place, suggesting human-to-human transmission. Organizations like WHO and the Center for Disease Control and Prevention (CDC) are monitoring the current H5N1 situation and will not officially proclaim the beginning of a pandemic until confirmed by their reference laboratories.

Has a vaccine been developed against the virus yet?

Yes, clinical trials of a Vietnam strain of H5N1 human vaccine have demonstrated safety and efficacy. Further work is required to determine the proper dosing and

potential boosting of adjuvants. The US Department of Health and Human Services (HHS) has placed an initial order for this vaccine and stands ready to order more once it is available. It remains to be seen, however, whether this vaccine will be effective against other H5N1 strains currently circulating, let alone against a pandemic strain that has undergone genetic change from the currently circulating virus. Once a new pandemic virus has emerged, large-scale production can begin of a more specific pandemic vaccine. Supplies sufficient to significantly impact a rolling pandemic may not be available for at least six months. Although the current global production capacity is inadequate for the expected vaccine needs, alternate and more efficient technologies for vaccine development are being vigorously pursued.

Will getting a flu shot this year afford any protection against a future pandemic avian influenza virus?

No. The annual influenza vaccine is targeted against specific influenza strains predicted from the previous year. Yearly seasonal flu shots are not even effective against next year's influenza strains, let alone against a future emerging pandemic strain. Of course MED encourages everyone to have the seasonal vaccine every year to prevent flu.

Are medications available to treat the viral infection?

At this time, two drugs in the neuraminidase inhibitor class, oseltamivir (Tamiflu) and zanamivir (Relenza), reduce the severity and duration of the seasonal influenza if administered within 48 hours after symptoms begin. Clinical data is limited for utilization of these drugs with H5N1 viral infections but laboratory data indicates that if administered early, the avian influenza virus will be susceptible. The H5N1 virus is resistant to the older antiviral drugs amantidine and ramantidine, so they are unlikely to work against an emerging human H5N1 strain. It is always possible, however, that the genetic reassortment producing a pandemic strain might confer susceptibility once again to these older drugs.

Primary restraints on stockpiling the neuraminidase inhibitors now involve a very limited production capacity and a prohibitively high price for many countries. Various countries have formed a rather long queue at the door of Roche Pharmaceuticals, currently the sole manufacturer of Tamiflu. Strong efforts are now underway to allow alternative production sources to ramp up across many nations.

The World Health Organization (WHO) recommended that countries begin to stockpile Tamiflu in April of 2005 when it declared a phase three interpandemic alert. WHO is also suggesting that countries maintain adequate supplies of antibiotics to treat what may occur as a secondary infection with the flu.

What will "social distancing" mean in the setting of an influenza pandemic?

We have learned from past pandemics that crowding will hasten infection with added surges stressing local healthcare capacity. For this reason, measures to decrease social interaction may become prudent such as school closures, curtailing public gatherings, and resorting to alternative work arrangements such as telecommuting. As infection rates heighten in communities, issues such as care for the sick and adequate food and water may become more important. Stockpiling of food and water is difficult to argue against, a pandemic being only one of several reasons.

Can a pandemic be prevented?

The answer is unclear. The best way to prevent a pandemic would be to eliminate the virus from birds, an unlikely scenario in the near future. As mentioned above there are theoretical models of prophylactically utilized antivirals near the start of a pandemic to reduce the emergence of a fully transmissible virus or delay its international spread and to gain time for vaccine development. The success of this strategy would depend upon excellent surveillance and logistics within the area and enforce movement restrictions in and out of the affected areas. The WHO expects to have a donated rapid-intervention stockpile of the drugs to implement this untested strategy although there are concerns over inadequate surveillance in likely affected countries.

What is the WHO recommending?

In August 2005, the WHO sent all countries information outlining recommended strategic actions to respond to the avian influenza pandemic threat. These actions aim to strengthen national preparedness, reduce opportunities for a pandemic virus to emerge, improve early warning systems, delay initial international spread, and to accelerate vaccine development.

Is the world adequately prepared?

No. The world is ill prepared to defend itself during a full-blown pandemic despite an advance warning of two years. Many countries have developed preparedness plans but many have not. On 11/02/2005, the HHS released the detailed final domestic plan for the US (see www.pandemicflu.gov).

What is being done in countries that have bird flu cases?

Most of the countries are working with WHO/OIE/FAO to attempt accurate surveillance and reporting with culling of large populations of infected and exposed poultry (chickens, ducks, turkeys). Those countries with cases of human bird flu are trying to isolate and quarantine (mostly via hospitalization) the infected and

potentially infected cases. They are sending test samples to reference labs for verification of infections with the H5N1. They are utilizing antiviral treatments and hospital intensive care therapy as indicated and available.

How do I decide if a family member or I might have avian influenza?

Ask questions of epidemiological nature: Do you live in a country with bird flu present in wild birds? In poultry? In humans? Have you traveled to areas where AI has been reported? Have you been to open air poultry or exotic bird markets? Have you had exposure to a human case? Have you recently plucked, played with or prepared (butchered) any type of poultry? Have you eaten improperly cooked, raw chicken or more exotic rice dishes made with raw poultry products such as duck's blood?

Ask questions about the symptoms of your illness:

Respiratory coughs, difficulty breathing, wheezing, fever, sore throat, nasal congestion, conjunctivitis, abdominal pain, recent watery diarrhea, vomiting, nose bleeds or bleeding gums?

If the answers to any of these questions are "yes", please call your health professional and discuss your illness rather than reporting to work.

Is there a laboratory test to diagnose Avian Influenza?

Some clinics in some countries have acquired test kits to test for seasonal influenza. These kits have a varying level of sensitivity but can help determine whether you may have influenza "A or B". If the "A" test is positive and other symptoms and epidemiological information suggests the possibility of avian influenza, other samples may need to be sent to an advanced reference lab to perform a definitive identification of the type of influenza virus. This is a highly sophisticated test that may require several days to complete. There are other basic blood tests that your caregiver may wish to perform. If the constellation of your epidemiological information, symptoms, physical examination and laboratory tests is suggestive for Avian Influenza you should begin treatment.

What precautions should I take if I live in an area affected by bird flu?

Avoid contact with live birds, chickens, ducks, turkeys and geese and their feces, feathers and pens. Children, in particular, should be warned and precautions enforced. Pet birds should not be kept. If preparing poultry, cook it well done before eating. Avoid cross contamination of other foods by use of separate kitchen utensils and surfaces exposed to raw poultry. Wash hands with soap and water after any poultry contact. Be sure, if possible, that poultry does not live near your housing area. Do not transport live or dead poultry even if it appears to be healthy. Avoid poultry products from areas of infected birds. If you must travel to infected areas, hand

washing and shoe and clothing cleaning should be an immediate priority. Be sure to wear gloves, a special N-95 mask, goggles and a disposable gown if you must be in contact with the birds/poultry. Observe yourself for the development of any respiratory or gastrointestinal symptoms after the visit and check your temperature for a week afterwards.

If I live in an affected area, are eating poultry and eggs safe and how should I prepare it safely?

In addition to what was said above, do not eat raw or soft-boiled eggs nor utilize them uncooked in food preparations. Cook all poultry thoroughly using a food thermometer to ensure that poultry reaches at least 180 degrees Fahrenheit. Eggs should be cooked solid throughout. Eggs, hands, knives, cutting boards and all counter tops may be washed with soapy water and sanitized with a solution of one-teaspoon chlorine bleach in a quart of water. <http://www.fsis.usda.gov>.